REMARKS

A check for the fees for a three month extension of time accompanies this response. Any fees that may be due in connection with the filing of this paper or with this application may be charged to Deposit Account No. 06-1050. If a Petition for Extension of Time is needed, this paper is to be considered such Petition.

A change in Power of Attorney to the undersigned and members of her firm has been filed under separate cover. An assignment to Receptor Biologix, the new owner of this application, has been executed and recordation will be effected.

Claims 15, 18-24, 26-32 and 57-59 are pending in this application. Claims 57-59 are added and claims 15, 21-24, 26, 27 and 30-32 are amended for clarity. Amended claims 15 and dependent claims find basis throughout the application. For example, basis can be found in the original claims in the parent application. Claims 57-59 find particular basis in original claims 15 and 16 in the instant application. Therefore, no new matter is added.

THE REJECTION OF CLAIM 27 UNDER 35 U.S.C. §112, FIRST PARAGRAPH

Claim 27 is rejected under 35 U.S.C. §112, first paragraph, as containing new matter because the claim recites a method in which the immunogenic composition is conjugated to an immunogenic carrier and a pharmaceutically acceptable carrier.

Reconsideration of the grounds for this rejection is respectfully requested in view of the amendments herein and the following remarks. Claim 27 is amended herein to correct the obvious typographical error and place "and" with "in," thereby obviating this ground for rejection.

THE REJECTION OF CLAIMS 15-29, 31-33 UNDER 35 U.S.C. §103(a)

Claims 15-29, 31-33 are rejected under 35 U.S.C. §103(a) as being unpatentable over allegedly admitted prior art (Background section) in view of Watson *et al.* (Cancer Research, 1996 (Watson I herein), or Int. J. Cancer, 1995 (Watson II herein)) or Gevas *et al.* (US Patent 5,607,676) because:

> [t]e instant claims are directed to method for treating a mammalian subject having excess gastric acid comprising the steps of administering to said subject, (a) a proton pump inhibitor; and (b) an immunogenic composition comprising a G17 peptide of SEQ ID NO: 1 or fragment thereof.

The Examiner urges that the Background Section, p. 1-2, or see Gevas *et al.*, col. 1-2, teaches that:

> administering proton pump inhibitors to subjects having excess gastric acid results in hypergastrinemia, *i.e.*, elevated level of gastrin peptides (such as

> G17 peptide), and that, in turn, hypergastrinemia leads to such complications as increased production of gastric acid, and gastric tumors. See Background Section, p. 1-2, or see Gevas et al, col. 1-2. Therefore, it is obvious that such side effects of proton pump blockers are undesirable and need to be treated or prevented.

The Examiner further states that each of Watson I and II teaches the use of the immunogen, Gastrimmune, which is composed of nine N-terminal residues of gastrin linked to immunogenic carrier, such as diphtheria toxoid, to raise anti-G17 antibodies, which reduce gastrin level in vivo, and that Gevas *et al.* (US Patent 5,607,676) teaches such immunogens to generate anti-gastrin antibodies, which reduce level of gastrin and inhibit hypergastrinemia related disorders. The Examiner concludes that it would have been:

> be prima facie obvious to one of ordinary skills in the art at the time the invention was made to be motivated to use the anti-gastrin immunogen of Gevas *et al.* or Watson *et al.* to reduce level of gastrin and inhibit hypergastrinemia- related disorders, because it would limit the side effects caused by administration of proton pump blockers.
>
> In regard to dependent claims 16-29, 31-33, if there are any differences between Applicant's claimed methods and that of the prior art, the differences would be appear minor in nature. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to determine all operable conditions for treatment of patient having hypergastrinemia and subsequent side effects, and determining such parameters as order of administration, target levels of gastrin, selection of particular inhibitors, are art recognized result-effective variables which would have been routinely determined and optimized in the art.

This rejection respectfully is traversed.

Relevant Law

In order to set forth a prima facie case of obviousness under 35 U.S.C. § 103: (1) there must be some teaching, suggestion or incentive supporting the combination of cited references to produce the claimed invention (ACS Hospital Systems, Inc. v. Montefiore Hospital, 732 F.2d 1572, 1577, 221 USPQ 329, 933 (Fed. Cir. 1984)) and (2) the combination of the cited references must actually teach or suggest the claimed invention. Further, that which is within the capabilities of one skilled in the art is not synonymous with that which is obvious. Ex parte Gerlach, 212 USPQ 471 (Bd. APP. 1980). Obviousness is tested by "what the combined teachings of the references would have suggested to those of ordinary skill in the art." In re Keller, 642 F.2d 413, 425, 208 USPQ 871, 881 (CCPA 1981), but it cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination (ACS Hosp. Systems, Inc. v Montefiore Hosp. 732 F.2d 1572, 1577. 221 USPQ 329, 933 (Fed. Cir. 1984)). "To imbue

one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher" W.L. Gore & Associates, Inc. v. Garlock Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983).

Under 35 U.S.C. §103, in order to set forth a case of prima facie obviousness, the differences between the teachings in the cited reference must be evaluated in terms of the whole invention, and the prior art must provide a teaching or suggestion to the person of ordinary skill in the art to have made the changes that would produce the claimed product. See, *e.g.*, Lindemann Maschinen-fabrik Gmbh v. American Hoist and Derrick Co., 730 F.2d 1452, 1462, 221 U.S.P.Q.2d 481, 488 (Fed. Cir. 1984). The mere fact that prior art may be modified to produce the claimed product does not make the modification obvious unless the prior art suggests the desirability of the modification. In re Fritch, 23 U.S.P.Q.2d 1780 (Fed. Cir. 1992); see, also, In re Papesh, 315 F.2d 381, 137 U.S.P.Q. 43 (CCPA 1963). In addition, if the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teachings of the references are not sufficient to render the claims prima facie obvious. In re Ratti, 270 F.2d 810, 123 USPQ 349 (CCPA 1959).

The claims

Claim 15 is directed to A method for treating a mammalian subject for hypergastrinemia by administering an immunogenic composition that contains a G17 peptide of SEQ ID NO: 1 or fragment thereof to thereby lower gastrin levels to treat the hypergastrinemia. Claims 18-21 recite the levels to which gastrin is lowered; claims 22, 23, and 26 recite that the subject has diseases consequent to hypergastrinemia; claim 24 recites that the treatment for hypergastrinemia is administered prior to development of a consequent disease; and claims 27-29 recite particulars regarding the immunogenic composition that is administered. Claims 57 recites that the treatment for hypergastrinemia reduces the effects thereof. Claims 58, 59 and 29-30 are directed to embodiments in which the treatment for hypergastrinemia is administered with a second agent selected from among a histamine receptor blocker and a proton pump inhibitor.

Hence, all of the claims are directed to methods for treatment of hypergastrinemia.

Differences between the cited references and the claims

Alleged admissions in the background section

The background section provides no teaching or admission that hypergastrinemia is a condition for treatment. The background section states that:

(1) "Around 90% of patients with pernicious anemia (PA) are hypergastrinemic and total gastrin levels can be up to forty times higher than normal levels." This is not a teaching that hypergastrinemia is a condition that should be treated

(2) The background continues and discusses gastrin biology and then states:

> There is a significant positive correlation between the degree of hypergastrinemia and the number of enterochromaffin-like (ECL) cells. However, the histological type of ECL cell hyperplasia is not dependent on the degree of hypergastrinemia as there is no significant difference in the gastrin levels in patients with linear or nodular hyperplasia. Once diagnosed, despite continuing elevated gastrin levels, the ECL cell hyperplasia appears to remain stable.

Again there is no teaching for treatment of hypergastrinemia. In fact, it states that there is no significant difference in gastrin levels in patients with linear or nodular hyperplasia and that the course of the disease is not correlated with gastrin levels.

(3) The background continues to discuss the relationship between ECL cell carcinoids, but provides no teaching for treating hypergastrinemia. The background continues discussing relationships betweens hypergastrinemia and other diseases, but again, there is no teaching for treatment of hypergastrinemia nor that hypergastrinemia causes any diseases. The background section states that there is no correlation between serum gastrin levels and gastric cancer in the majority of patients.

Hence, the background section provides no admission that "hypergastrinemia leads to such complications as increased production of gastric acid, and gastric tumors" as urged by the Examiner, and certainly provides not admission that treatment of hypergastrinemia was previously known.. The background section fails to teach methods for the treatment of hypergastrinemia, an essential element of all pending claims.

Gevas *et al.*

Gevas *et al.* similarly provides not teaching for treatment of hypergastrinemia, and fails to cure this deficiency. Gevas *et al.* is directed to a method for treatment of "gastrin-induced disorders." Gevas *et al.* (col. 2, lines 52-59) states:

> [t]his invention provides a novel immunological approach to the control and regulation of gastrin induced disorders such as peptic ulcers. According to the invention, antibodies are induced in the patient by active immunization with

> immunogens that selectively target specific forms of gastrin. Alternatively, the patient can be passively immunized with anti-gastrin antibodies specific for certain forms of gastrin.

Gevas *et al.* does not teach or suggest that hypergastrinemia is a disorder nor does it teach any methods for treating hypergastrinemia. In fact, the word hypergastrinemia does not appear in Gevas *et al*

Watson I and Watson II

Each of these references teaches the immunogen, Gastrimmune and its use for treating various tumors. Neither reference teaches methods for treatment of hypergastrinemia.

Watson I describes the effect of Gastrimmune on gastrin-sensitive colorectal tumors. It does not teach or suggest anything regarding treating hypergastrinemia. Watson II describes the effect of Gastrimmune on the *in vivo* growth of rat colon tumor cells, and concluded that "tumor-induced levels" of gastrin were reduced about 40% (see, page 882, column 2). The levels of gastrin only are mentioned in the context of cancer. No mention is made that would suggest treatment of hypergastrinemia as a condition.

The combination of teachings of the cited references does not result in the claimed methods

As discussed above, the instant claims are directed to methods for the treatment of hypergastrinemia. None of the cited references, singly nor in any combination thereof, teaches or suggests methods for the treatment of hypergastrinemia. None recognize hypergastrinemia as a health condition worthy of treatment. Absent such teaching in any of the cited references and alleged admission, the combination of teachings of the cited references and alleged admission cannot and does not result in the instantly claimed methods for treatment of hypergastrinemia.

To combine these references to result in the claimed methods relies on the improper use of hindsight

"To imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher" W.L. Gore & Associates, Inc. v. Garlock Inc., 721 F.2d 1540, 1553, 220 USPQ 303, 312-13 (Fed. Cir. 1983).

It is only the application at issue that teaches or suggests that hypergastrinemia is a condition that needing treatment. Therefore, the Examiner has failed to set forth a *prima facie* case of obviousness.

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In view of the, amendments and remarks herein, reexamination and allowance of the application are respectfully requested.

Respectfully submitted,

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